Combination treatment also attenuated the increase in blood lactate levels observed in the Compound J monotherapy group ($p = 0.01$ for 0 h timepoint, Figure 2).

This study indicates that combination treatment with an insulin secretagogue and an FBPase inhibitor provides significantly improved glycemic control over treatment with either agent alone. Improved glycemic control is likely to result in a reduced incidence of the complications associated with NIDDM. In addition, in this acute setting combination treatment attenuated a side effect associated with FBPase inhibitor therapy, blood lactate elevation. In a chronic setting this attenuation is more pronounced.--

REMARKS

In accordance with 37 C.F.R. §1.121, a marked up copy of the presently amended paragraphs of the specification is appended hereto. Deletions to the originally filed text are noted by bracketing. These amendments are being made merely to transfer Figures 1 and 2, originally included on page 317 of the specification, to a separate sheet of drawings. Accordingly, no new matter is added with these amendments.

Respectfully submitted,

BROBECK, PHLEGER & HARRISON LLP

Dated: 10-11-2001

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MARKED UP VERSION OF AMENDED PORTIONS OF THE SPECIFICATION

Results: In pilot studies it was established that glyburide and Compound J were maximally efficacious in this model at doses of 100 and 300 mg/kg, respectively. In the current study, both glyburide and Compound J suppressed the rise in blood glucose levels induced by the oral glucose load, with compound J lowering blood glucose to below baseline levels (see Figure 1 [below]). Combination treatment was better than either monotherapy as indicated by the enhanced reduction in the area under the curve (AUC) of blood glucose during the initial 4 hours post drug administration:

Table 11:

Treatment	AUC glucose, mg/dL*h
Control	1463±99
Glyburide	1324±132
Compound J	1121±82
Combination	895±74

Combination treatment also attenuated the increase in blood lactate levels observed in the Compound J monotherapy group ($p = 0.01$ for 0 h timepoint, Figure 2).

This study indicates that combination treatment with an insulin secretagogue and an FBPase inhibitor provides significantly improved glycemic control over treatment with either agent alone. Improved glycemic control is likely to result in a reduced incidence of the complications associated with NIDDM. In addition, in this acute setting combination treatment attenuated a side effect associated with FBPase inhibitor therapy, blood lactate elevation. In a chronic setting this attenuation is more pronounced.